

REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS OF AMENDMENTS

Claims 1-11, 13-15 and 17-29 were pending in this application when last examined.

Claims 2-11, 13-15, and 19-29 were withdrawn as non-elected subject matter.

Claims 1, 17 and 18 were examined on the merits and stand rejected.

Claim 1 has been amended to incorporate the subject matter of claim 6. Claim 1 has been further amended to move subject matter from the preamble of the claim into the body of the claim.

Minor editorial revisions have been made to the claims to better conform to U.S. claim form and practice. Such revisions are non-substantive and not intended to narrow the scope of protection. Such revisions include: replacing the "characterized by" language with "wherein"; revising the claim language throughout to provide proper antecedent basis for the claim terminology; and removing the "preferably", "type" and the "like" language and adding such back as new dependent claims.

New dependent claims 30-34 have been added that correspond to the subject matter of the inappropriate

"preferably" and "for example" language removed from claims 5 and 8.

No new matter has been added by the above claim amendments.

Claim 6 has been canceled without prejudice or disclaimer thereto. Applicants reserve the right to file continuation or divisional application on any canceled subject matter.

Claims 1-5, 7-11, 13-15, and 17-34 are pending upon entry of this amendment.

Applicants have amended the withdrawn claims to be consistent with the amendments to the elected and examined claims. Kindly consider the possibility of rejoinder of the withdrawn claims upon a determination of allowance of the elected claims in accordance with US rejoinder practice.

The specification is amended to include appropriate section headings to conform to US practice. No new matter has been added.

Applicants are submitting the present amendment without prejudice to the subsequent prosecution of claims to some or all of the subject matter which might be disclaimed by virtue of this response (although none is believed to be) and explicitly reserve the right to pursue some or all of such subject matter in divisional or continuation applications.

Applicants thank the Examiner for the careful examination of this case and respectfully request reconsideration of the case, as amended. Below Applicants address the rejections in the Office Action and explain why the rejections are not applicable to the pending claims as amended.

## II. OBJECTION TO THE SPECIFICATION

The specification is objected to for containing the minor informality noted at page 2 of the Office Action. In reply, Applicants have amended the specification to include appropriate section headings where needed to thereby overcome this objection. Withdrawal of the objection is therefore rejected.

## III. INDEFINITENESS REJECTION

Claim 1 was rejected under 35 USC § 112, second paragraph, as being indefinite for the term "substantial" for the reasons noted on page 3 of the Office Action.

This rejection is respectfully traversed. For the sole purpose of expediting prosecution and not to acquiesce in the rejection, the claims have been amended to remove the term "substantial", thereby overcoming this rejection. As such, the rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

#### IV. OBVIOUSNESS REJECTION

Claims 1 and 17-18 were rejected under 35 U.S.C. § 103(a) as being obvious over MORCOL et al. (WO 02/064112) in view of KELLER (US 6,726,924) and BAKER et al. (US 6,534,018) for the reasons noted on pages 4-5 of the Office Action.

This rejection is respectfully traversed as applied to the amended claims.

It is well established that to support a *prima facie* case of obviousness, the Office must provide a rationale showing that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions to yield predictable results. KSR International Co. v. Teleflex Inc., 550 U.S. \_\_\_, \_\_\_, 127 S. Ct. 1727, 82 U.S.P.Q.2d 1385, 1395 (2007); and M.P.E.P., Eighth Ed., Rev. 6 (September 2007) at § 2143.02.

To start, Applicants wish to draw the Examiner's attention to the following points:

MORCOL et al. (WO 02/064112) disclose a system for the oral administration comprising a therapeutic agent, said agent being, in particular, encapsulated in calcium phosphate, wherein these capsules may be surrounded by a casein membrane (see p. 11-12). It is mentioned that the corresponding complex is designed to protect the therapeutic agent in the acidic environment of the stomach before releasing said agent into the small intestine

(last line of p. 11 - 1.2, p. 12). MORCOL et al. also disclose the use of PEG as surface modifying agent (p. 19, l. 12-13), said agent modifying the surface of the calcium phosphate particles (also referred to as core).

However, there is no indication in MORCOL et al. that the core is hydrophilic nature as required in amended claim 1.

Further, it should also be noted that the surface modifying agents of MORCOL et al. are used to coat and adhere a therapeutic agent to the formed particle core (p. 17, l.1-3). However, there is no indication relating to the modification of the outer surface of said particle core. More particularly, MORCOL et al. fails to disclose the nature of the bonds between the surface modifying agents (chemical species of claim 1) and the particle core surface (hydrophilic matrix of claim 1).

Indeed, it is noted that the chemical species modifying the outer surface of the hydrophilic matrix of the system according to the amended claim 1 of the present application are attached to said matrix by weak bonds, such that said bonds can be detached from the matrix by contact with the microvilli present in the intestine and during the passage through the intestinal barrier. The detachment of the chemical species from the matrix thus allows the latter to return to its essentially hydrophilic nature.

Thus, MORCOL et al. does not disclose the attachment of chemical species to the matrix via weak bonds that give the

vector an essentially lipophilic nature as required in amended claim 1.

Furthermore, the system of MORCOL et al. delivers the therapeutic agent in the small intestine (p. 12, 1.1-2), but not in the blood as required in amended claim 1 of the present application.

As mentioned by the Office, MORCOL et al. do not teach the particles being contained in an additional lipophilic compound. Thus, MORCOL et al. do not disclose the use of a lipophilic medium as being an additional protection from the external aqueous medium.

It is important to note that these additional protections (lipophilic compound for gastric protection and chemical species for modifying the surface of the matrix) are essential to allow the pharmacologically active substance to pass through the intestinal barrier and then to be available in the blood as required in amended claim 1. Thus, the present invention is based on a system for the administration of a pharmacologically active substance to pass from the intestinal lumen to the blood (see p. 6, 1. 1-6) of the present application (see also p. 16, 1. 7-14).

However, as previously mentioned MORCOL et al. do not provide such a system as the active substance is delivered in the small intestine but not in the blood (p. 12, 1. 1-2).

For these reasons, it is believed that MORCOL et al. fail to disclose or suggest each and every element of amended independent claim 1.

The secondary references of KELLER and BAKER et al. fail to remedy the deficiencies of MORCOL et al.

KELLER (US 6,726,924) discloses the encapsulation of an active substance in a liposome, said liposome being in particular protected with a gelatine shell, which may also be coated with a cellulosic polymer (col. 4, l. 26-30).

BAKER et al. (US 6,534,018) disclose lipidic vesicles comprising an active substance encapsulated in either the aqueous core or within the lipidic bilayer of said vesicles (col. 25, l. 20-24).

However, there is no indication in either reference relating to the bonds between the matrix containing the active substance and a chemical species modifying the outer surface of said matrix.

As mentioned above, the nature of said bonds is essential to have the active substance delivered in the blood without any leaking of said substance. Again, it is noted that independent claim 1 has been amended to reflect this essential aspect.

For these reasons, it is believed that the rejection falls because the combination of MORCOL et al., KELLER, and BAKER et al. fail to disclose or suggest each and every element of

amended independent claim 1. In conclusion, the claims are not obvious over MORCOL et al., in view of KELLER and BAKER et al.

Further, it is noted that even if the skilled artisan were to combine and follow the teachings in the cited references, the skilled person would obtain a system for administration of an active substance in the small intestine and not in the blood as required in claim 1. None of the cited documents describe the modification of the matrix containing the active substance. In this sense, it could be said that the cited references actually teach away from the vector of claim 1.

In this regard, it is well established that a prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984). M.P.E.P., Eighth Ed., Rev. 6 (September 2007) at § 2141.02, VI. Moreover, a prior art reference that "teaches away" from the claimed invention is a significant factor to be considered in determining obviousness. M.P.E.P., Eighth Ed., Rev. 6 (September 2007) at § 2145, X, D, 1.

For the above reasons, it is believed that the combination of MORCOL et al., in view of KELLER and BAKER et al. actually teaches away from the claims.

In the prior art references, the active substance is delivered in the intestine, whereas with the system of the claims



the product which is delivered in the intestine is the matrix containing the active substance. The modification of the outer surface of the matrix is then an additional protection of the active substance, which leads to the passage of said substance in the blood.

For these reasons, it is believed that amended independent claim 1 and all claims dependent thereon (including claims 17-18 and withdrawn claims 2-5, 7-11, 13-15, 19-29) are novel and nonobvious over the cited references.

Therefore, Applicants respectfully submit that the above-noted 103(a) obviousness rejection is untenable and should be withdrawn.

#### V. CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the application is in condition for allowance and notice to that effect is hereby requested. If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

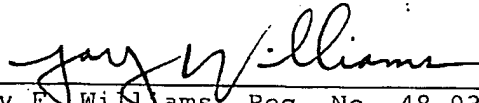
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Respectfully submitted,

YOUNG & THOMPSON



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Jay F. Williams, Reg. No. 48,036  
Customer No. 00466  
209 Madison Street, Suite 500  
Alexandria, VA 22314  
Telephone (703) 521-2297  
Telefax (703) 685-0573  
(703) 979-4709

JFW/fb